REMARKS

This Amendment and Remarks are filed in response to the Non-Final Office Action dated February 26, 2006 wherein all currently pending claims 38-48 are rejected.

Claim Rejections under 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, Examiner states that in claim 38, support is not found in the specification for "cartilesions or defects" (bridging lines 1 and 2). The specification discloses defects as lesions, and not defects as an alternative to lesions. It is suggested "or defects" be deleted.

Applicants disagree, however, to advance the prosecution, Applicants amended claim 38 to delete the language "or defects" from claim 38.

In step f) (lines 9-12 of the step), support is not found in the specification for applying cyclic hydrostatic pressure

followed by applying static atmospheric pressure to the matrix of step e) after perfusing as required in step f) (lines 7-8 of the step). According to the specification, applying cyclic hydrostatic pressure followed by applying a static atmospheric pressure occurs during perfusing required in step f). It is suggested line 9 of step f) be amended by before "applying" inserting --- during said perfusing, ---, and canceling "of step e)".

Applicants disagree, however, to advance the examination, Applicants amended claim 38, step f), as suggested by the Examiner.

Bridging the last two lines of step f), support is not found in the specification for "said protocol repeated for from about one day to about ninety days". The specification does not disclose repeating a protocol. Additionally, the time of about one day to about ninety days is disclosed in the specification as a time for applying the static atmospheric pressure, and not a time for repeating a protocol. It is suggested "said protocol repeated for from about one day to about ninety days" be deleted.

Applicants disagree but amended claim 38 as suggested.

Examiner also argues that support is not found in the specification for the alternatives of "sponge, scaffold, hone or honeycomb-like lattice" as required in line 2 of claim 40. The specification discloses a sponge matrix or honeycomb matrix as being a scaffold, and not a scaffold being an alternative to a honeycomb or sponge matrix. In line 2, it is suggested "a sponge, scaffold, honeycomb or honeycomb-like lattice" be replaced with ---- in the form of a sponge or honeycomb---.

Applicants disagree, however, in an effort to advance the prosecution, Applicants amended claim 40 as suggested.

With these amendment, rejections of claims 38 and 40 under 35 USC 112,first paragraph are overcome.

Claim Rejections under 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of claim 38 is unclear as to the relationship of providing an implantable construct and providing a means for formation of a superficial cartilage layer to steps a)-h) subsequently required. Defining the method in general terms in the preamble before setting forth specific steps confuses the method performed. It is unclear how the general description of the method in the preamble defines the method in addition to steps a)-h).

Additionally, reciting "lesions or defects" (bridging lines 1 and 2) is unclear as to defects that are not lesions since the specification fails to disclose defects that are not lesions. It is suggested the preamble be replaced with -- A method for treatment of cartilage lesions comprising steps:---

Applicants disagree, however, to expedite the examination, Applicants amended claim 38 as suggested.

To be clear, the claim should be further amended as follows.

Line 2 of a), insert --- stem --- before "cells", and cancel "could" and insert --- can ---.

Line 1 of step b), insert --- stem --- before "cells".

Line 1 of step c) cancel "isolated", and insert --- stem before "cells".

Line 2 of step c), after "solution", insert --- to obtain a

suspension --- .

Line 1 of step e), cancel "a" and insert ---the---.

Lines 2 and 4 of step f), insert --- stem --- before "cells".

In lines 7-14 of step f), it is unclear as to when applying cyclic hydrostatic pressure and static atmospheric pressure are applied relative to perfusing. The specification indicates that cyclic hydrostatic pressure and static atmospheric pressure are applied during perfusing, and this should be clear in the claim. It is suggested in line of step f) be amended as set forth above in the 112, first paragraph rejection.

In line 13 of step f), there is not antecedent basis for "said protocol". Additionally, it is uncertain as to steps that would be repeating the protocol since the specification fails to describe repeating a protocol. It is suggested the portion of the step from the comma in line 13 to "days" in line 14 be canceled.

In line 5 of step h), there is not clear antecedent basis in the previous steps for "the superficial". It is suggested the claim recite "a superficial".

Applicants disagree, however, for clarity reasons, to meet Examiner's rejections and to expedite the examination, Applicants amended claim 38 as suggested by the Examiner.

In claim 40, "honeycomb-like" is uncertain as to meaning and scope. Being "like" a honeycomb is relative and subject depending on ones interpretation of material that is like a honeycomb. Claim 40 is further unclear as to a matrix that is a scaffold as an alternative to a sponge, honeycomb and honeycomb-like lattice since the specification fails to describe a scaffold as an alternative as to a sponge, honeycomb and honeycomb-like lattice.

Applicants disagree. However, claims 40 is amended as suggested.

Claim 47 is unclear as to the meaning of "grows into" as an alternative to "provides the same type of". The claim is unclear

as
10 to what the cartilage layer grows into, and the specification does not provide any more description than the claim as to what the cartilage layer grows into.

Claim 48 is unclear as to the difference in in vitro and ex vivo since in vitro encompasses ex vivo and the converse.

Applicants disagree, however, to expedite the prosecution, applicants canceled the *ex vivo* language from claim 48.

With these amendment, is it believed that all rejections under 35 USC 112, second paragraph are overcome.

Claim Rejections - 35 USC § 103

Claims 38 and 40-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al (6,528,052 Bl) in view of Wise et al (American Surgeon) and Rhee et al (5,475,052, and if necessary in further view of Rhee et al 5,565,519).

Examiner argues that Smith et al disclose regeneration of cartilage tissue in a cartilage defect by seeding a scaffold or support (col 9, line 30) in vitro with isolated chondrocytes (col 9, lines 22-33), applying intermittently hydrostatic pressure followed by a recovery period (col 4, lines 37-41 and col 7, line 30 to col 8, line 8) to obtain the scaffold or support containing chondrocytes or cartilage tissue, and implanting the resultant seeded scaffold or support or cartilage tissue in the cartilage defect (col 9, lines 31-33).

Examiner further argues that Wise et al disclose using a collagen-polyethylene glycol sealant to seal leaks after liver transplantation.

Examiner further adds to the combination references Rhee et al ('052) as disclosing using for implant applications a collagen-synthetic polymer matrix that can be a collagen-polyethylene glycol cross-linked matrix (col 16, line 59 and col 24, line 29), and disclose methylated collagen (col 16, line 29) as a chemically modified collagen that can be the collagen of the

collagen-synthetic polymer matrix. The chemically modified collagen has an altered charge (col 16, line 26) and is more or less optically clear (col 16, line 32) and Rhee et al ('519) disclosing using a collagen-polyethylene glycol conjugate for ophthalmic applications (cols 9-20).

Examiner concludes that it would have been obvious to seal a defect after implanting cartilage tissue or a scaffold or support seeded with chondrocytes in a defect as disclosed by Smith et al by using a collagen-polyethylene glycol sealant as suggested by Wise et al using this sealant and Rhee et al ('052) using a collagen-polyethylene glycol cross-linked matrix for implant applications. Methylated collagen is taught by Rhee et al ('052) (col 16, line 29) as a modified collagen that can be used as the collagen of the collagen-polyethylene glycol cross-linked matrix for results of altered charge and optically clear collagen, and it would have been obvious to use a methylated collagen-polyethylene glycol cross-linked matrix as the collagen-polyethylene glycol sealant suggested by Wise et al. It would been obvious that sealing the defect after the implant will be advantageous to prevent contamination and infection at the site of the defect. The cartilage tissue or seeded scaffold produced by Smith et al before implanting is inherently a construct. If needed, Rhee et al ('519) would have further suggested using a collagen-polyethylene glycol sealant from disclosing using a collagen-polyethylene glycol conjugate for ophthalmic applications. Applying a hydrostatic pressure and static atmospheric pressure as in step f) is suggested by Smith et al disclosing applying intermittent hydrostatic pressure and a recovery period. Perfusing as claimed would have been obvious during culturing to produce cartilage tissue and culture seeded chondrocytes to supply nutrients for cells. The parent application does not antedate Wise et al since the presently claimed invention is not disclosed in the parent application.

Applicants disagree. The combination of the above references, as Examiner is suggesting is not obvious. Examiner combines four unrelated references from unrelated fields.

Applicants submit that to render a claim obvious, the prior art must teach each element of the claims, there must be motivation to combine the references, and there must be some expectation of success if the references are combined.

The inventions concerns orthopedic surgery and treatment. Wise reference concerns gastric surgery and treatment of bile leakage. Rhee '052 concerns providing collagen-synthetic materials for matrices. Rhee '519 concerns ophthalmic application of chemically modified collagen-synthetic polymer conjugates. To combine these four references to provide ground for rejections of the instant claims can only be made in hindsight of the instant invention.

Person skilled in the art would have no reason to utilize the sealant of Wise, or Rhee '052 (who does not even disclose the use as a sealant) or the ophthalmic preparation fo Rhee '519 for use as a covering layer over the lesion site implanted with a construct containing activated chondrocytes with any expectation that there would be formation of the superficial cartilage layer during the time of healing when the utilized adhesive and the construct is biodegraded. Since the consequence of the Applicants' method is unexpected and unforeseeable, it cannot be obvious.

Additionally, Examiner always argues that such formation and development of superficial cartilage layer is inherent.

Applicants disagree. The combination of the references is artificial, made in hindsight and would not be made without knowledge of the Applicants invention. There are hundreds of sealants and adhesives that could be used and no particular reason to use PEG-methylated collagen or any other. There is no particular reason to use the sealant at all. The reason Examiner

is giving is not rational. There is no need during the arthroscopic surgery to protect the lesion or construct from contamination or outside environment or to prevent infection. The surgery is performed in sterile conditions and any infection or contamination following the surgery would be very serious. To use the sealant for these purposes would be counterintuitive to a person skilled in the art because neither infection or contamination is expected to happen during surgery and the construct is never exposed to the outside environment.

Method of the invention, including a combination of steps a)-h), in claim 38 leads to formation of the superficial cartilage layer. Such element is not taught or suggested from any cited prior art. Thus, the prior art does not teach each element of the claims. There is no motivation to combine the references. All references relate to different subject matter and to the different field. There is no reason for sealant to be used at all during the arthroscopic surgery and no reason to pick-up just one single sealant, i.e. methylated collagen-PEG, among all other available sealants. There was no any expectation that the superficial cartilage layer might be formed since there was no knowledge or recognition of possibility of the formation and growth of the superficial cartilage layer from the combination of the construct containing activated cells with the specific adhesive material. Person skilled in the art could not have expected or predicted that if such combination is made, the development and formation of the superficial cartilage layer will follow. It was solely due to observation on the part of inventors that when the method steps and material used were combined, the membrane that resembles the synovial membrane normally covering the joint cartilage could be formed. Therefore, there was no expectation of success if the references were combined.

It is respectfully submitted that the claim 38 and dependent

claims 39-47 are not obvious. Rejection should be withdrawn. Examiner is respectfully requested to withdraw the rejection and let the claims passed to issue.

Double Patenting

Claims 38-48 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 11 of U.S. Patent No. 7,217,294 in view of Smith et al (6,528,052).

The patent claims require a method of repairing a cartilage lesion by putting a bottom sealant in the lesion, lesion a matrix implant, and applying a layer of top sealant over the defect.

It would have been obvious to seed the matrix with chondrocytes in vitro before implanting, and apply intermittent hydrostatic pressure and a recovery period as disclosed by Smith et al since the matrix seeded with chondrocytes would have been expected to form new cartilage sooner than using the matrix without the seeded chondrocytes.

Applicants disagree, however, to expedite the examination, Applicants herewith submit the fully executed Terminal Disclaimer disclaiming the terminal portion of the patent 7,217,294. With such submission, Double Patenting rejection is overcome and should be withdrawn.

SUMMARY

In summary, claims are amended to overcome rejections under 35 USC 103, 112, first and second paragraph. Arguments are provided to overcome rejections under 35 USC 103. With the amendments and arguments submitted herein, all claims are in conditions for immediate allowance. Notice of Allowance is respectfully solicited.

Respectfully submitted,

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